

LS990031  
patent application

**IN THE CLAIMS**

36. (currently amended) A device manufactured in accordance with the method of claim 84, [it-a]said device having a plurality of well structures for the parallel processing of a plurality of independently controlled molecular reactions and at least one of: a heating element, cooling element and temperature monitoring element associated with each well structure, [the-improvement] said device further comprising:

- (a) a substantially monolithic device structure wherein said plurality of well structures are defined within material comprising a plurality of green-sheet layers, said green-sheet layers comprising particles selected from the group consisting of ceramic particles, glass particles and glass-ceramic particles; and
- (b) said substantially monolithic structure further comprising thermal insulating material separating said well structures.

37. (previously added) The apparatus of claim 36, wherein said molecular reaction comprises a polymerase chain reaction.

38. (previously added) The apparatus of claim 36, wherein said thermal conducting layer of the well structures comprises a resistive heater.

39. (previously added) The apparatus of claim 38, wherein said well structures comprise a thermally conductive material and are separated by thermal insulating material.

40. (previously added) The apparatus of claim 39, wherein said thermal insulating material comprises at least one of glass, silicon, ceramic and polymeric material.

LS990031  
patent application

41. (previously added) The apparatus of claim 38, wherein said thermal conducting material comprises at least one material selected from the group consisting of substantially undoped silicon, substantially modified polymeric material, silver, silver palladium, copper, nickel-molybdenum, platinum and gold; and said thermal insulating material comprises at least one material selected from the group consisting of glass, silicon, ceramic, polymeric material or air contained in an air channel positioned substantially proximal to said well structure.

42. (previously added) The apparatus of claim 36, wherein said well structures are coated with a compound that effectively enhances biocompatibility between the components of the molecular reaction and at least one of said thermal insulating and conducting material comprising the well structures.

43. (previously added) The apparatus of claim 42, wherein said coating compound comprises parylene.

44. (previously added) The apparatus of claim 36, wherein said integrated heating system comprises a thin film resistive heater.

45. (previously added) The apparatus of claim 36, wherein said integrated heating system comprises a metal wire resistive heater.

46. (previously added) The apparatus of claim 45, wherein said metal wire resistive heater is substantially integrated into the thermal insulating material comprising the supporting substrate.

47. (previously added) The apparatus of claim 36, wherein said integrated heating system utilizes column-and-row electrical addressing.

48. (previously added) The apparatus of claim 36, wherein said integrated heating system utilizes substantially individual electrical addressing.

49. (previously added) The apparatus of claim 36, wherein said means for cooling each well structure comprises a passive cooling system.

LS990031  
patent application

50. (previously added) The apparatus of claim 36, wherein said means for cooling each well structure comprises an active cooling system.

51. (previously added) The apparatus of claim 50, wherein said active cooling system comprises an integrated cooling system.

52. (previously added) The apparatus of claim 51, wherein said integrated cooling system comprises at least one of a metal plate, an array of metal discs and a thermo-electric cooler, wherein said integrated cooling system is suitably adapted for thermal contact with each of said well structures.

53. (previously added) The apparatus of claim 36, wherein said means for monitoring said temperature of said molecular reactions in each well structure comprises at least one of an integrated optical and electrochemical sensor system.

54. (previously added) The apparatus of claim 36, further comprising sealed well structures.

55. (previously added) The apparatus of claim 54, wherein said well structures are sealed using a layer of mineral oil.

56. (previously added) The apparatus of claim 54, wherein said well structures are sealed using a cover.

57. (previously added) The apparatus of claim 56, wherein said cover further comprises means for heating said well structures.

58. (previously added) The apparatus of claim 56, wherein said means for heating said well structures comprises an integrated heating system.

59. (previously added) The apparatus of claim 36, wherein said thermal insulating material comprises a polymeric material and said means for monitoring the temperature of contents contained in each well structure comprises an integrated resistive thermal detector which is suitably adapted for molding into said polymeric material.

LS990031  
patent application

60. (previously added) The apparatus of claim 36, wherein said thermal insulating material comprises polymeric material and said means for monitoring the temperature of the contents of each well structure comprises a thermocouple which is suitably adapted for molding into said polymeric material.

61. (previously added) The apparatus of claim 36, wherein each of said heaters comprise coils forming loops around each of said well structures along a length of said well structures.


62. (previously added) The apparatus of claim 36, further comprising electrical connections to said well structures distributed three-dimensionally within said substantially monolithic structure.

63. (previously added) The apparatus of claim 36, further comprising conductive pathways extending along and into the device, wherein said pathways are suitably adapted to make electrical connection to at least one of said heaters, coolers and temperature monitors.

64. - 83. (withdrawn)

LS990031  
patent application

**84. (New)** A method for making the device of claim 36, said method comprising the steps of:

- 
- (a) providing a plurality of green-sheet layers, said green-sheet layers including particles selected from the group consisting of ceramic particles, glass particles and glass-ceramic particles;
  - (b) sintering said green-sheet layers to produce a substantially monolithic device structure; said monolithic structure comprising a plurality of separated well structures separated by thermal insulating material;
  - (c) providing a heating element associated with each well structure;
  - (d) providing a cooling element associated with each well structure; and
  - (e) providing a temperature monitoring element associated with each well structure.

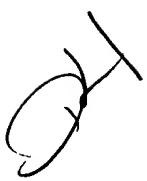
**85. (New)** The method of claim 84, wherein said thermal conducting layer of the well structures comprises a resistive heater.

**86. (New)** The method of claim 85, wherein said well structures comprise a thermally conductive material and are separated by thermal insulating material.

**87. (New)** The method of claim 86, wherein said thermal insulating material comprises at least one of glass, silicon, ceramic and polymeric material.

**88. (New)** The method of claim 85, wherein said thermal conducting material comprises at least one material selected from the group consisting of substantially undoped silicon, substantially modified polymeric material, silver, silver palladium, copper, nickel-molybdenum, platinum and gold; and said thermal insulating material comprises at least one material selected from the group consisting of glass, silicon, ceramic, polymeric material or air contained in an air channel positioned substantially proximal to said well structure.

LS990031  
patent application

- 
- 89. (New)** The method of claim **84**, further comprising the step of coating said well structures with a compound that effectively enhances biocompatibility between the components of the molecular reaction and at least one of said thermal insulating and conducting material comprising the well structures.
- 90. (New)** The method of claim **89**, wherein said coating compound comprises parylene.
- 91. (New)** The method of claim **84**, wherein said integrated heating system comprises a thin film resistive heater.
- 92. (New)** The method of claim **84**, wherein said integrated heating system comprises a metal wire resistive heater.
- 93. (New)** The method of claim **92**, further comprising the step of substantially integrating said metal wire resistive heater into the thermal insulating material comprising the supporting substrate.
- 94. (New)** The method of claim **84**, further comprising the step of sealing said well structures.
- 95. (New)** The method of claim **94**, wherein said well structures are sealed using a layer of mineral oil.
- 96. (New)** The method of claim **94**, wherein said well structures are sealed using a cover.
- 97. (New)** The method of claim **96**, wherein said cover further comprises means for heating said well structures.
- 98. (New)** The method of claim **96**, wherein said means for heating said well structures comprises an integrated heating system.
- 99. (New)** The method of claim **84**, wherein said thermal insulating material comprises a polymeric material and said step of monitoring the temperature of

LS990031  
patent application

contents contained in each well structure comprises an integrated resistive thermal detector which is suitably adapted for molding into said polymeric material.

100. (New) The method of claim 84, wherein said thermal insulating material comprises polymeric material and said step of monitoring the temperature of the contents of each well structure comprises a thermocouple which is suitably adapted for molding into said polymeric material.

101. (New) The method of claim 84, wherein each of said heaters comprise coils forming loops around each of said well structures along a length of said well structures.

102. (New) The method of claim 84, further comprising the step of forming electrical connections to said well structures distributed three-dimensionally within said substantially monolithic structure.

103. (New) The method of claim 84, further comprising the step of forming conductive pathways extending along and into the device, wherein said pathways are suitably adapted to make electrical connection to at least one of said heaters, coolers and temperature monitors.

*\* The preceding claims and the formatting of this Response & Amendment have been presented in accordance with the proposed revisions to 37 CFR § 1.121, which the office plans to adopt by July 2003.*